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10/542,435	05/02/2006	Jeffrey D. Rothstein	JHU2090-1	2771

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1609	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/542,435	ROTHSTEIN ET AL.	
	Examiner	Art Unit	
	Stacey MacFarlane	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) *1, 5-6 8,11-12, 18 and 20-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-7,9-17 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 July 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. In the reply filed on April 17, 2007, Applicant's election of Group III, Claims 2-7, 9-17 and 19 and the following species is acknowledged: detecting levels of glutamate transport; wherein the GTRAP3-18 target molecule is a glutamate transporter; and wherein the glutamate transporter is GLAST/EAAT1. Claims 2-4, 7, 9-10, 13-17 and 19 read upon the elected species and will be considered upon their merits. An examination of compounds that modulate the GTRAP3-18 nucleic acid transcript, polypeptide or activity was found to **not** be an undue burden upon the examiner, therefore the species election for Claim 2 was withdrawn.

2. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 1, 5-6 8,11-12, 18 and 20-44, are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim.

Priority

3. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. This application is a 371 of PCT/US04/01162 filed January 18, 2004 which claims benefit of provisional 60/440,717, filed January 17, 2003.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims are drawn to a method of identifying a compound that binds GTRAP3-18, wherein the compound is capable of treating a glycosylation disorder, specifically neurological or psychiatric disorders selected from the group consisting of the list of Claims 16 or 17.

5. The nature of the invention is broad, drawn to methods for the identification of any compound capable of binding GTRAP3-18, and defining those compounds as modulators of glycosylation, and then use of those compounds for the treatment of glycosylation disorders. Firstly, one of ordinary skill in the art would not easily recognize all compounds that are capable of binding GTRAP3-18 as glycosylation modulators. For example the specification describes protein interaction between GTRAP3-18 and rEAAT3/EAAC1 (Pg. 7, line 22-24) but one of ordinary skill in the art would not easily recognize excitatory amino acid transporters as modulators of cellular glycosylation. Furthermore, the claims directed toward the compound as capable of effectively treating all glycosylation disorders is based on this assertion because the disclosure provides no

working example showing successful treatment of any disease using the compound of the assay. Given the state of the art for a single compound to be capable of treating all of the disorders of the claims, the quantity of experimentation required to develop GTRAP3-18 binding proteins as effective treatments for disease would be undue in the absence of any direction or guidance from the specification. Thus, the claims fail to enable one skilled in the art to use the invention

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 2, 4, 7, 9, 13, 14-16 and 19 are rejected under 35 U.S.C. 102(a) as being anticipated by Butchbach et al. Journal of Neurochemistry 84: 891-894, published February 15, 2003, as evidenced by Sáez-Valero et al. (Journal of Neurology, Neurosurgery and Psychiatry, 69: 664-667, 2000) and Fassbender et al. (Proc. Natl. Acad. Sci. U.S.A. 98, 5856–5861, 2001).

Claim 2 is drawn to methods for identifying a compound comprising (1) contacting a cell which expresses GTRAP3-18 with a test compound and (2) assaying the ability of the test compound to modulate the expression of GRTAP3-18 transcript, protein or activity. Dependent claims further recite wherein the modulation of GTRAP3-18 transcript, protein or activity is determined by detecting levels of glutamate (Claim 4) or amino acid transport (Claim 7) by a GTRAP3-18 target molecule; wherein that GTRAP3-18 target molecule is the instantly-elected glutamate (Claim 9) amino acid transporter (Claim 13), and specifically the elected species of GLAST/EAAT1 (Claim 10). Further, the method wherein the cell contacted is a neuronal cell (Claim 19) and the compound is capable of treating a glycosylation associated neurologic or psychiatric disorder (Claims 14-16).

Butchbach et al. teach the identification of compounds (methyl-β-cyclodextrin and retinoic acid) which when applied to neuronal cells (rat hypothalamic neuron cultures; pg. 891 paragraph titled "Reagents and cell lines") modulates GTRAP3-18 protein expression (methyl-β-cyclodextrin; Figure 1b) and activity (retinoic acid; Figure 1a). Butchbach identifies glutamate as an "excitatory amino acid" (first line of the article) and teaches modulation as determined by detecting the levels of glutamate transport in the cell (Figure 1a) as mediated via the excitatory amino acid transporter EAAT3, teaching the "GTRAP3-18 target molecule" of Claims 9. Sáez-Valero et al. identify Alzheimer's disease as a "glycosylation accociated disorder" (abstract) and Fassbender, et al. teach that the compound methyl-β-cyclodextrin of the Butchbach reference is capable of treating Alzheimer's disease by lowering toxic amyloid products (pg. 5856 Column 2,

line 17). Thus, teaching the compound is "capable of treating a glycosylation associated disorder" (Claim 14), wherein the disorder is "neurologic" (Claim 15) and the "Alzheimer's disease" of Claim 16.

6. Claims 2, 4, 7, 9-10 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Lin et al. Nature 410: 84-88, published March 1, 2001. Claims are drawn to methods for identifying a compound comprising (1) contacting a cell which expresses GTRAP3-18 with a test compound and (2) assaying the ability of the test compound to modulate the expression of GTRAP3-18 transcript, protein or activity. Dependent claims further recite wherein the modulation of GRTAP3-18 transcript, protein or activity is determined by detecting levels of glutamate (Claim 4) or amino acid transport (Claim 7) by a GTRAP3-18 target molecule; wherein that GTRAP3-18 target molecule is the a amino acid or glutamate transporter (Claims 9, 13), and specifically the elected species of GLAST/EAAT1 (Claim 10).

The Lin prior art teaches antisense oligomers reduce GTRAP3-18 protein expression and activity (Figure 3d) as determined by glutamate transport via the co-expressed excitatory amino acid transporter, EAAC1. The Lin reference also teaches cells contacted with retinoic acid increase GTRAP3-18 protein expression (Figure 4a) and decrease GTRAP3-1 activity as determined by glutamate transport via coexpressed EAAC1, thus, teaching the specific "GTRAP3-18 target molecule" of Claims 4, 7 and 9-10. Further, the reference teaches method wherein the cells contacted are neuronal cells (Figures 3e and 4e). Therefore, the reference teaches detection of the amino acid

transport, and specifically glutamate, recited in Claims 4 and 7, as well as the instantly-elected GTRAP3-18 target molecule of Claims 4, 7, 9-10 and 13.

7. Claims 2, 4, 7, 9, 13 and 19 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent 6808893 ('893 Patent).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claims are drawn to methods for identifying a compound comprising (1) contacting a cell which expresses GTRAP3-18 with a test compound and (2) assaying the ability of the test compound to modulate the expression of GTRAP3-18 transcript, protein or activity. Dependent claims further recite wherein the modulation of GRTAP3-18 transcript, protein or activity is determined by detecting levels of glutamate (Claim 4) or amino acid transport (Claim 7) by a GTRAP3-18 target molecule; wherein that GTRAP3-18 target molecule is the a amino acid or glutamate transporter (Claims 9, 13), and specifically the elected species of GLAST/EAAT1 (Claim 10).

The '893 Patent teaches antisense oligomers (Figure 8A-C) reduce GTRAP3-18 protein expression and activity as determined by glutamate transport via the co-expressed excitatory amino acid transporter, EAAC1. The '893 Patent further recites,

"Retinoic acid induces a large increase in GTAP3-18 expression ... A significant decrease in glutamate transport activity paralleled the increase of GTRAP3-18 protein level" (¶ 219). Therefore, the prior art patent teaches the detection of the level of glutamate, or amino acid, transport recited in Claims 4 and 7, and the specific "GTRAP3-18 target molecule" of Claims 4, 7, 9-10 and 13. Furthermore, the '893 Patent discloses GTRAP3-18 to be expressed in neuronal cells (¶ 13), thus, teaching the method of Claim 19.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 3 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lin et al. as applied to claims 2, 4, 7, 9-10 and 13 above, and further in view of Hirabayashi and Kasai, Journal of Chromatography B 771: 67-87, published May 5, 2002. Claims are drawn to methods for identifying a compound comprising (1) contacting a cell which expresses GTRAP3-18 with a test compound and (2) assaying the ability of the test compound to modulate the expression of GTRAP3-18 transcript, protein or activity, wherein the modulation of GRTAP3-18 transcript, protein or activity is determined by detecting levels of glycosylation of a GTRAP3-18 target molecule, the GTRAP3-18 target molecule being an amino acid or glutamate transporter.

The Lin prior art teaches antisense oligomer and retinoic acid modulation of GTRAP3-18 protein expression and activity as determined by glutamate transport via coexpressed EAAC1. The Lin reference does not teach detection of GTRAP3-18 protein and activity modulation by detecting the level of glycosylation of a GTRAP3-18 target molecule. The Hirabayashi and Kasai reference discloses a variety of techniques (i.e. mass spectrometry, 2-D/3-D mapping and ConA-agarose column purification) for quantification of glycosylated proteins and discloses these methods are essential for a understanding the effects of glycosylation, which is "involved in numerous biological phenomena, such as cell development, differentiation, implantation, morphogenesis, tumor metastasis, microbe infection, etc." and that, in cell culture models, mutations in the pathways of glycosylation demonstrate no altered phenotypes, whereas genetic defects in these pathways lead to termination of development at the embryonic stage (pg. 68, column 2, lines 5-13). It would be obvious to one of ordinary skill in the art to apply the methods of Hirabayashi and Kasai to the methods described in Lin et al. A skilled artisan would be motivated to combine because quantification of glycosylation allows for a fuller investigation of the role a protein plays in cell function.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacey MacFarlane whose telephone number is (571) 270-3057. The examiner can normally be reached on Monday-Thursday 6:30AM-4:00 PM & ALT. Fridays, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mary Mosher can be reached on (571) 272-0906. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MARY MOSHER
SUPERVISORY PATENT EXAMINER

6-8-07